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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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08/434,105

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DAVID A FISCHHOFF

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MONSANTO COMPANY

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ST. LOUIS, MO 63167

EXAMINER

KUBELIK, ANNE R

ART UNIT

PAPER NUMBER

1638

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 08/434,105	Applicant(s) FISCHHOFF ET AL.	
	Examiner Anne R. Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 47-141 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 47-141 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 47-141 are pending.
2. The examiner thanks Applicant for sending the copies of the prosecution documents from 07/959,506, 07/476,661 and 07/315,355, which are currently designated lost by the Office.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. The rejection of claims 47-70, 81-82, 84-85, 87-88, 93-100, 102-104, 106-107, 109-119 rejected under 35 U.S.C. 103(a) as being unpatentable over Beremand et al (1989, US Patent 4,888,282) in view of Fischhoff et al (1987, Bio/Technol. 5:807-813) is withdrawn in light of Applicant's arguments with respect to the effective date of invention of the instant application.
5. The rejection of claims 47-199 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure that is not enabling is withdrawn in light of Applicant's arguments.
6. The rejection of claims 47-58 and 67-68 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 71-72 of copending Application No. 10/102,469 is withdrawn in light of Applicant's amendment of the claims of 10/102,469.
7. The rejection of claims 47-119 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement presented starting on pg 5 of the Office action mailed 30 May 2007 is withdrawn.

Claim Rejections - 35 USC § 112

8. Claims 47-141 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Dependent claims are included in all rejections. Due to Applicant's amendment of the claims, the rejection is modified from the rejection set forth in the Office action mailed 30 May 2007, as applied to claims 47-119. Applicant's arguments filed 30 November 2007 have been fully considered but they are not persuasive.

The portion of the previous rejection relating to "designing a nucleotide sequence" in part (a) of claims 113 and 117 is withdrawn.

(a) Neither the instant specification nor the originally filed claims appear to provide support for modifying any insecticidal protein coding sequence derived from any *Bacillus* species in claims 47, 51, 55, 59, 63, 67, 112, 113, 117 and 119. Neither the instant specification nor the originally filed claims appear to provide support for the concept of the insecticidal protein coding sequence being from any *Bacillus* species. Nowhere in the specification or the originally filed claims is the starting material from any *Bacillus* species, only *B. thuringiensis*. The specification indicates that insecticidal protein coding sequences only from *Bacillus thuringiensis* were considered (see pg 16, lines 28, to pg 22, line 24, and originally filed claims 3, 9, 13, and 30).

Applicant urges that original claim 18 recites "derived from *B.t.k.*" and claim 40 recites "derived from a *Bacillus thuringiensis*" (response pg 18).

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This is not found persuasive because neither *Bacillus thuringiensis* k. nor *Bacillus thuringiensis* provide support for derivation from any *Bacillus* species.

Applicant urges that “derived from” indicates origin, but does not restrict to a wild-type sequence, and numerous sequences in Examples 1-3 were “derived from *Bacillus*” (response pg 19).

This is not found persuasive because the examples only provide support for those fragments from Cry endotoxin genes, not for any sequence from any gene from any *Bacillus* species.

There are at least 192 *Bacillus* species other than *B. thuringiensis*, including *B. acidicer*, *B. acidicola*, *B. acidopullulyticus*, *B. acidovorans*, *B. aeolius*, *B. aeris*, *B. aestuarii*, *B. agaradhaerens*, *B. akibai*, *B. alcaliinulinus*, *B. alcalophilus*, *B. algicola*, *B. alkalidiazotrophicus*, *B. alkalitolerans*, *B. alkalogaya*, *B. alveayuensis*, *B. amiliensis*, *B. amyloliquefaciens*, *B. aquimaris*, *B. arbutinivorans*, *B. arseniciselenatis*, *B. arsenicus*, *B. asahii*, *B. atrophaeus*, *B. axarquiensis*, *B. azotoformans*, *B. badius*, *B. baekryungensis*, *B. barbaricus*, *B. bataviensis*, *B. benzoovorans*, *B. bhargavae*, *B. bogoriensis*, *B. boroniphilus*, *B. butanolivorans*, *B. caldolyticus*, *B. caldotenax*, *B. caldovelox*, *B. carboniphilus*, *B. casamancensis*, *B. catenulatus*, *B. cellulosityticus*, *B. cereus*, *B. anthracis*, *B. mycoides*, *B. chaganniensis*, *B. cibi*, *B. circulans*, *B. clarkii*, *B. clausii*, *B. coagulans*, *B. coahuilensis*, *B. cohnii*, *B. coniferum*, *B. danangensis*, *B. decisifrondis*, *B. decolorationis*, *B. deramificans*, *B. djibelorensis*, *B. drementensis*, *B. edaphicus*, *B. endophyticus*, *B. farraginis*, *B. fastidiosus*, *B. ferrariarum*, *B. firmus*, *B. flavocaldarius*, *B. flexus*, *B. foraminis*, *B. fordii*, *B. fortis*, *B. fucosivorans*, *B. fumarioli*, *B. funiculus*, *B. galactosidilyticus*, *B. gelatini*, *B. gibsonii*, *B. ginsenggisoli*, *B. ginsengihumi*, *B.*

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granadensis, *B. hackensackii*, *B. halmapalus*, *B. halodurans*, *B. halophilus*, *B. hemicellulosilyticus*, *B. herbersteinensis*, *B. horikoshii*, *B. horti*, *B. humi*, *B. hwajinpoensis*, *B. idriensis*, *B. indicus*, *B. infantis*, *B. infernus*, *B. insolitus*, *B. intermedius*, *B. israeli*, *B. jeotgali*, *B. koreensis*, *B. krulwichiae*, *B. lentus*, *B. licheniformis*, *B. litoralis*, *B. longiquaesitum*, *B. longisporus*, *B. luciferensis*, *B. macauensis*, *B. macroides*, *B. macyae*, *B. malacitensis*, *B. mangrovensis*, *B. mannanyticus*, *B. marisflavi*, *B. massiliensis*, *B. megaterium*, *B. methanolicus*, *B. mojavensis*, *B. mucilaginosus*, *B. muralis*, *B. nealsonii*, *B. nematocida*, *B. niabensis*, *B. niacini*, *B. nitritophilus*, *B. novalis*, *B. odysseyi*, *B. ohbensis*, *B. okhensis*, *B. okuhidensis*, *B. oleronius*, *B. olivae*, *B. oryzae*, *B. oshimensis*, *B. panaciterrae*, *B. patagoniensis*, *B. pichinoty*, *B. plakortiensis*, *B. pocheonensis*, *B. polyfermenticus*, *B. polygoni*, *B. pseudalcaliphilus*, *B. pseudofirmus*, *B. pseudomegaterium*, *B. pseudomycoides*, *B. psychrodurans*, *B. psychrosaccharolyticus*, *B. psychrotolerans*, *B. pumilus*, *B. pycnus*, *B. qingdaonensis*, *B. racemilacticus*, *B. ruri*, *B. salarii*, *B. saliphilus*, *B. samanii*, *B. schlegelii*, *B. selenatarsenatis*, *B. selenitireducens*, *B. senegalensis*, *B. shackletonii*, *B. shandongensis*, *B. silvestris*, *B. simplex*, *B. siralis*, *B. smithii*, *B. solfatarensis*, *B. soli*, *B. sonorensis*, *B. sporothermodurans*, *B. subterraneus*, *B. subtilis*, *B. szutsauensis*, *B. tequilensis*, *B. thermantarcticus*, *B. thermoalkalophilus*, *B. thermoamyloliquefaciens*, *B. thermoamylovorans*, *B. thermocloaceae*, *B. thermoproteolyticus*, *B. thermoterrestris*, *B. thermozeamaize*, *B. thioparus*, *B. tipchiralis*, *B. vallismortis*, *B. vedderi*, *B. velezensis*, *B. vietnamensis*, *B. vireti*, *B. viscosus*, *B. vortex*, *B. wakoensis*, and *B. yunchengensis*. There is no support for any of these species in the specification.

Applicant urges that the application makes it clear that the invention was intended to be applicable to any protein, citing the paragraph spanning pg 16-17 (response pg 19-20).

This is not found persuasive because the paragraph spanning pg 16-17 provide support for *Bacillus thuringiensis* crystal proteins, non-plant proteins, and plant proteins. It does not provide support for the subset of proteins from other *Bacillus* species.

(b) Neither the instant specification nor the originally filed claims appear to provide support for the concept of producing a coding sequence that is substantially devoid of polyadenylation signal sequences but not substantially devoid of ATTTA sequences and vice versa, as in claims 47, 51, 55, 59, 63, 67, 112, 113, 117, 119, 120, 122, 124, 126 and 128. In original claims 13 and 33 the sequences are substantially devoid of both.

Applicant urges that support is found on pg 22-24, original claim 1-2 and example 1 (response pg 20-21).

This is not found persuasive because original claims 1-2 only provides support for reducing the occurrence of polyadenylation signals, not for making the sequence “substantially devoid” of them. Further, claims 1-2 do not provide support for producing a coding sequence that is substantially devoid of ATTTA sequences but not substantially devoid of polyadenylation signal sequences. Pg 23, lines 3-4, and the Example only provide support if “partial removal” and removal of three polyadenylation signals are the same thing as “substantially devoid”.

(c) Neither the instant specification nor the originally filed claims appear to provide support for the starting material being sequences encoding portions of any two or more insecticidal polypeptides, as in claims 55 and 67. The only multiple starting sequences originally conceived are specific B.t. insecticidal proteins.

Neither the instant specification nor the originally filed claims appear to provide support for the starting material or protein being hybrids of at least any two B.t. insecticidal proteins or their coding sequences, as in claims 59 and 91-92.

Neither the instant specification nor the originally filed claims appear to provide support for the insecticidal protein being any insecticidal fusion, as in claims 113-114.

Applicant urges that Example 3 provides examples of fusions (response pg 21).

This is not found persuasive because the example only provides support for a particular HD1/HD73 fusion; the other fusions were fusions of HD73 synthetic coding sequence with HD73-wild-type coding sequence. The Example does not provide support for fusions involving any protein or other *Bacillus* insecticidal proteins.

(d) Neither the instant specification nor the originally filed claims appear to provide support for using coding sequences for an amino-terminal chloroplast transit peptides or a secretion signal sequence attached to any protein, as in claim 108.

Applicant urges that support is found on pg 32 and Examples 10-11 (response pg 22).

This is not found persuasive because pg 32 and the Examples only provide support for the transit and signal peptides attached to Bt crystal proteins. There is no support for attachment to any *Bacillus* protein or a protein from any source other than Bt.

(e) Neither the instant specification nor the originally filed claims appear to provide support for making any *Bacillus* derived structural gene containing no more than one, seven or two ATTTA and/or Table II polyadenylation sequences or none at all as in claims 71-76. The specification, in Examples 1 and 4, only describes doing this in specific *B. thuringiensis* sequences, not in any one.

Applicant urges that Example 2 provides support for making HD-1 devoid of PolyA signals and having only 1 ATTTA sequence; further support is on pg 23, 39 and 42 (response pg 23).

This is not found persuasive because Example 2 only provides support for a particular combination in HD-1. Claims 72-76 are not original. Pg 23 and 39 do not provide support for those specific numbers of signals/sequences in any *Bacillus* protein, any *Bacillus thuringiensis* Cry protein or any *Bacillus* insecticidal protein. Pg 42 only discusses specific modifications to HD-1, and does not provide support for the particular numbers in any *Bacillus* protein or any *B. thuringiensis* Cry protein.

The following rejections are new:

(f) Neither the instant specification nor the originally filed claims appear to provide support for the starting material being any protein or any *Bacillus* protein with a starting sequence having an A+T content of 62% in claims 79-80 and 136. The specification on pg 21, line 5, and pg 91, lines 8-9, only says Bt genes have a 62% A+T content.

(g) Neither the instant specification nor the originally filed claims appear to provide support for the concept of the starting material being the coding sequence for any insecticidal protein, as in claim 126. The specification indicates that only insecticidal protein coding sequences from *Bacillus thuringiensis* were considered (see pg 16, lines 28, to pg 22, line 24, and originally filed claims 3, 9, 13, and 30).

(h) Neither the instant specification nor the originally filed claims appear to provide support for the starting material being sequences encoding portions of any two or more polypeptides, as in claim 128.

Thus, such a phrases and concepts constitute NEW MATTER. In response to this rejection, Applicant is required to point to support for the phrases and concepts or to cancel the new matter.

9. Claims 47-112, 117-118 and 120-141 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

The rejection is modified from the rejection set forth in the Office action mailed 30 May 2007, as applied to claims 47-58 and 63-111. Applicant's arguments filed 30 November 2007 have been fully considered but they are not persuasive.

Applicant's arguments with respect to the previous rejection over the terms "reduced" and "reducing" are persuasive and that portion of the previous rejection is withdrawn.

(a) Claims 63-68, 112, 117-118 and 126-129 are indefinite in their recitation of "substantially devoid". "Substantially" is a relative term, that renders the claim indefinite - what level of reduction is considered "substantial"?

Applicant urges that because the claims recite "substantially devoid", the question of what level of reduction is considered "substantial" is not relevant (response pg 31).

This is not found persuasive because the method involves making a gene that is substantially devoid. The level of reduction that is "substantial" is relevant because it sets an upper limit on that feature in the structural gene.

Applicant urges that provides plain meanings of “devoid” and “substantially”, saying that “substantially devoid” modestly broadens “devoid” to mean one or a few sequences (response pg 32).

This is not found persuasive because the upper limit of “a few” is not clear.

Applicant urges that Example 2 makes a gene with no ATTTA and one polyA sequence (response pg 32).

This is not found persuasive because this example does not define an upper limit on “substantially devoid”. How many polyA or ATTTA sequences can be in the final coding sequence? If one removes one ATTTA sequence in a sequence with 100, would that be encompassed by the claim? Would removal of 50? 90? 95? The specification does not define the phrase.

Applicant urges that the MPEP in section 2173.05(b), part D cites cases in which “substantially” is definite (response pg 32-33).

This is not found persuasive because unlike in the first example, the specification provides no such guidelines. Wild-type HD-1 appears to have five ATTTA sequences (Fig 2); in Example 1, two were deliberately modified (at bases 419 and 1305), leaving three others (at bases 246, 506, and 1196). Is the resulting sequence “substantially devoid” of ATTTA sequences? Does removal of fewer than half of the sequences constitute “substantially devoid”? Would removal of only one of the HD-1 ATTTA sequences? What is the upper limit of “substantially devoid”? One of skill in the art would not know what “substantially devoid” means in this recitation.

The following rejections are new:

(b) Claims 47, 51, 55, 120, 122, and 124 are indefinite in their recitation of “reducing the number of said ATTTA sequences or the number of said polyadenylation signal sequences in the coding sequence by substituting sense codons for codons in the coding sequence”. The codons in the coding sequence would already be sense codons, and substituting any sense codon for one in the starting sequence would not necessarily reduce the number of ATTTA or polyadenylation sequences; only substitution with specific sense codons would do so.

(c) Claims 47, 51, 55, 120, 122, and 124 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: making the structural gene comprising a coding sequence that encodes the protein in step (a). As currently written there is no connection between the starting material of part (a) and the making step (c) except the substituted codons - the rest of the codons of the coding sequence of step (a) are not necessarily involved in step (c). A similar disconnect between the steps is seen in claims 59 and 63.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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Anne Kubelik, Ph.D.

February 20, 2008

/Anne R. Kubelik/

Primary Examiner, Art Unit 1638